Individual Safety Report

3659942-7-00-01

by user-facilities, and manufacturers for ATORY reporting.

APPROVED BY FDA ON 03/06/98

Mfr report # 253146

UF/Dist. report #

FDA Use only

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted]	or 17 YEARS	☐ female	155 lbs
In confidence	Date of birth: 13-FEB-1983	☒ male	or 70.3 kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- ☐ death (mo/day/yr) / /
- ☐ life threatening
- ☐ hospitalization inital or prolonge
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☒ other: MEDICALLY SIGNIFICANT

3. Date of event (mo/day/yr): NOV / 2 / 2000 E

4. Date of this report (mo/day/yr): JAN / 31 / 2001

5. Describe event or problem

THIS SPONTANEOUS CASE, REPORTED BY A DERMATOLOGIST, CONCERNS A 17 YEAR OLD MALE PATIENT WHO EXPERIENCED INCREASED BLOOD EOSINOPHILS, ABNORMAL LIVER FUNCTION TESTS, INCREASED CREATINE KINASE (CK), THE PRESENCE OF ANTINUCLEAR ANTIBODY (ANA), INCREASED BLOOD CHOLESTEROL, DECREASED WHITE BLOOD CELL COUNT (WBC DEC), DECREASED GRANULOCYTE COUNT AND DECREASED BLOOD NEUTROPHIL COUNT DURING THE USE OF ACCUTANE (ISOTRETINOIN) FOR ACNE AND TYLENOL (PARACETAMOL) FOR AN UNSPECIFIED INDICATION.

THE PATIENT HAS A NEGATIVE FAMILIAL HISTORY AND A NEGATIVE HISTORY FOR SMOKING, ALCOHOL USE, DRUG ABUSE AND ALLERGIES. HE HAS NO CONCOMITANT DISEASE.
27 JUL 2000: ACCUTANE THERAPY COMMENCED ORALLY AT 30 MG DAILY.
UNKNOWN DATE: TYLENOL THERAPY COMMENCED (ROUTE AND DOSING REGIMEN UNKNOWN).
7 SEP 2000: THE PATIENT'S ABSOLUTE NEUTROPHIL COUNT WAS LOW AT 1747 CELLS/MCL (NORMAL: 1800 - 8000).

CONTINUED

6. Relevant tests/laboratory data, including dates

ABS_NEUTROPHIL_COUNT
7-SEP-2000
LAB RESULT: 1747
NORMAL RANGE: 1800-8000
CELLS/MCL.

ANTI_NUCLEAR_AB

CONTINUED

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Medical History Text
THE PATIENT HAS A NEGATIVE FAMILIAL HISTORY AND A NEGATIVE HISTORY FOR SMOKING, ALCOHOL USE, DRUG ABUSE AND ALLERGIES. HE HAS NO CONCOMITANT DISEASE.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 ACCUTANE CAPSULES (ISOTRETINOIN)
#2 TYLENOL (ACETAMINOPHEN)

2. Dose, frequency & route
#1 30 MG DAILY ORAL
#2 UNK

3. Therapy dates (if unk, give duration) from/to (or best estimate)
#1 27-JUL-2000 / UNK
#2 UNK

4. Diagnosis for use (indication)
#1 ACNE
#2 UNKNOWN

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☒ doesn't apply

6. Lot # (if known)
#1 UNK
#2 UNK

7. Exp. date (if known)
#1 UNK
#2 UNK

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☒ doesn't apply

9. NDC # for product problems only (if known)
#1 NA #2 NA

10. Concomitant medical products and therapy dates (exclude treatment of event)
UNK

G. All manufacturers

1. Contact Office-name/address

GLOBAL DEVELOPMENT
HOFFMANN-LA ROCHE INC.
340 KINGSLAND STREET
NUTLEY, NJ 07110-1199

2. Phone Number: (973) 562-3523

3. Report source (check all that apply)
- ☐ foreign
- ☐ study
- ☐ literature
- ☐ consumer
- ☒ health professional
- ☐ user-facility
- ☐ company representative
- ☐ distributor
- ☐ other:

4. Date received by manufacturer: JAN / 19 / 2001

5. (A)NDA# 18-662
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #: NA

7. Type of report (check all that apply)
- ☐ 5 - day
- ☒ 15 - day
- ☐ 10 - day
- ☐ periodic
- ☒ initial
- ☐ follow-up #

8. Adverse event term(s)
BLOOD EOSINOPHILS INCREASED +++
ABNORMAL LIVER FUNCTION TESTS
CK INCREASED
ANA PRESENT
BLOOD CHOLESTEROL INCREASED
WBC DEC
GRANULOCYTE COUNT DECREASED
+++ adverse event that generated submission

9. MFR. report number: 253146

CONTINUED

E. Initial reporter

[redacted]

FEB 2 2 2001

CONTINUED

2. Health professional? ☒ yes ☐ no

3. Occupation: DOCTOR OF MEDICINE

4. Initial reporter also sent report to FDA ☐ yes ☐ no ☒ unk

FDA 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

E-Indicates estimated date or dose, P-Indicates partial date

FEB 1 2001

B.5. Describe event or problem - continued

25 SEP 2000: THE PATIENT DEVELOPED ABNORMAL
LIVER FUNCTION TESTS (ELEVATED).
30 OCT 2000: THE PATIENT'S SGOT WAS HIGH AT 478 U/L (0 - 42), SGPT HIGH AT 155 U/L
(0 - 48) AND ACETAMINOPHEN LEVEL < 10 MG/L (10 - 20).
UNKNOWN DATES: THE ACCUTANE AND TYLENOL THERAPIES WERE DISCONTINUED AND THE PATIENT
WAS REFERRED TO A GASTROINTESTINAL SPECIALIST. AN ULTRASOUND OF THE LIVER WAS
NEGATIVE.
2 NOV 2000: THE PATIENT'S SGOT AND SGPT LEVELS WERE CONSIDERED TO HAVE IMPROVED,
ALTHOUGH THEY REMAINED HIGH AT 147 U/L (NORMAL: 20 - 57) AND117 U/L (21 - 72)
RESPECTIVELY. HIS CHOLESTEROL LEVEL WAS HIGH AT 223 MG/DL (140 - 200) AND CK HIGH
AT 1703 IU/L (55 - 170). THE ACETAMINOPHEN LEVEL WAS 4 UG/ML
(10 - 30). HIS WBC WAS LOW AT 3.5 THOUSAND/MM3 (4.8 - 10.8) WITH GRANULOCYTES LOW
AT 45.5% (50 - 70) AND EOSINOPHILS HIGH AT 5.7 % (0 - 4).
6 NOV 2000: THE PATIENT'S SGOT AND SGPT LEVELS WERE 30 U/L (0 - 42) AND 41 U/L (0
- 48) RESPECTIVELY. HIS ANTINUCLEAR ANTIBODY TITER WAS 1:40 (REFERENCE RANGE: <
1:40 = NEGATIVE, 1:40 - 1:80 = LOW ANTIBODY LEVEL,
> 1:80 = ELEVATED ANTIBODY LEVEL).
THE OUTCOME OF THE EVENTS INCREASEDBLOOD EOSINOPHILS, INCREASED CREATININE KINASE,
ANA PRESENT, INCREASED BLOOD CHOLESTEROL, DECREASED WBC, DECREASED GRANULOCYTE
COUNT AND DECREASED BLOOD NEUTROPHIL COUNT WAS UNKNOWN.
THE REPORTING DERMATOLOGIST DESCRIBED THE CAUSALITY AS POSSIBLE FOR ABNORMAL LIVER
FUNCTION TESTS AND ACCUTANE BUT ALSO STATED THAT THE PATIENT TOOK LARGE AMOUNTS OF
TYLENOL AND THAT SHE FELT THE LIVER ENZYMES WERE ELEVATED AS A RESULT OF THIS.
THE COMPANY CONSIDERED THE EVENTS BLOOD EOSINOPHILS INCREASED, ABNORMAL LIVER
FUNCTION TESTS AND CREATINE KINASE INCREASED TO BE MEDICALLY SIGNIFICANT.

B.6. Relevant tests/laboratory data - continued

6-NOV-2000
LAB RESULT: 1.4
ANA TITER REFERENCE RANGES: < 1:40 = NEGATIVE, 1:40 - 1:80 = LOW ANTIBODY LEVEL,
> 1:80 = ELEVATED ANTIBODY LEVEL

CHOLESTEROL
2-NOV-2000
LAB RESULT: 223 mg/dL
NORMAL RANGE: 140-200 mg/dL

CPK
2-NOV-2000
LAB RESULT: 1703
NORMAL RANGE: 55-170

EOSINOPHILS
2-NOV-2000
LAB RESULT: 5.7 %
NORMAL RANGE: 0-4 %

GRANULOCYTES
2-NOV-2000
LAB RESULT: 45.5 %
NORMAL RANGE: 50-70 %

LIVER FUNCTION TESTS
25-SEP-2000
ELEVATED. NO SPECIFIC VALUES PROVIDED.

SGOT
30-OCT-2000
LAB RESULT: 478 U/L
NORMAL RANGE: 0-42 U/L

SGOT
2-NOV-2000
LAB RESULT: 147 U/L
NORMAL RANGE: 20-57 U/L

SGOT
6-NOV-2000
LAB RESULT: 30 U/L
NORMAL RANGE: 0-42 U/L

SGPT
30-OCT-2000
LAB RESULT: 155 U/L
NORMAL RANGE: 0-48 U/L

SGPT
2-NOV-2000
LAB RESULT: 117 U/L
NORMAL RANGE: 21-72 U/L

SGPT
6-NOV-2000
LAB RESULT: 30 U/L
NORMAL RANGE: 0-48 U/L

TEST_METHOD
30-OCT-2000
ACETAMINOPHEN LEVEL - < 10 MG/L (10 - 20).

TEST_METHOD
2-NOV-2000
ACETAMINOPHEN LEVEL - 4 UG/ML (10 - 30).

ULTRASOUND SCAN
LIVER - NEGATIVE.

WBC
2-NOV-2000
LAB RESULT: 3.5
NORMAL RANGE: 4.8-10.8
LAB UNITS: THOUSAND/MM3.

E.1. Initial reporter (Name, address & phone #) - continued

PHON[redacted]

G.8. Adverse event term(s) - continued

BLOOD NEUTROPHIL COUNT DECREASED